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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/009,584	05/21/2002	David M. Livingston	20363-012	1758
7590	03/23/2005		EXAMINER	
Mintz Levin Cohn Ferris Glovsky & Popeo One Financial Center Boston, MA 02111			GUZO, DAVID	
			ART UNIT	PAPER NUMBER
			1636	

DATE MAILED: 03/23/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/009,584	LIVINGSTON ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	David Guzo	1636	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) Responsive to communication(s) filed on 07 September 2004 and 17 December 2004.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) Claim(s) 1-7 and 25-32 is/are pending in the application.  
 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.  
 5) Claim(s) 1-4, 6, 25 and 32 is/are allowed.  
 6) Claim(s) 26-31 is/are rejected.  
 7) Claim(s) 5 and 7 is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
     Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
     Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                                   | Paper No(s)/Mail Date. _____  |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
|  | 6) <input type="checkbox"/> Other: _____                                    |

### Detailed Action

The Sequence Listing filed 9/7/04 is acceptable and has been entered.

### 35 USC 102 Rejections

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 26 and 28-30 are rejected under 35 U.S.C. 102(e) as being anticipated by Berkenstam et al.

Applicants claim an *in vitro* method of identifying a compound that modulates a transcriptional response to hypoxia in a cell, said method comprising: providing a candidate compound; contacting said candidate compound with a cell or the extracellular environment of a cell containing a hypoxia-responsive promoter or an endogenous hypoxia-responsive gene; subjecting the cell or the extracellular environment to hypoxic conditions; and assessing a transcriptional response of the cell to the hypoxic conditions, wherein an increase or decrease in the transcriptional response to hypoxia in the cell in the presence of the candidate compound compared to the transcriptional response to hypoxia in a cell in the absence of the candidate compound indicates that the candidate compound modulates the transcriptional

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response to hypoxia. The transcriptional response can be expression of a reporter gene under the control of a hypoxia-responsive promoter or an endogenous hypoxia-responsive gene and the reporter gene can encode green fluorescent protein (GFP) or luciferase.

Berkenstam et al. (US 6436654, issued 8/20/02, effective filing date of 11/20/1998, see whole document, particularly the Abstract; column 7, lines 44-67; column 8, lines 1-23; Claims 1, 5-8, 20, 22-26, Examples 5, 8) recites an *in vitro* method of identifying a compound that modulates a transcriptional response to hypoxia in a cell (such as COS7 cells), said method comprising providing a candidate compound; contacting said compound with the cell containing a hypoxia-responsive promoter (i.e. a erythropoietin hypoxia-responsive element) operably linked to a reporter gene (such as luciferase or GFP); subjecting the cell to hypoxic conditions; and assessing a transcriptional response of the cell to the hypoxic conditions wherein changes in the transcriptional response (i.e. changes in expression of the reporter gene) indicates that the candidate compound modulates a transcriptional response to hypoxia. Berkenstam et al. therefore teaches the claimed invention.

### **35 USC 103(a) Rejections**

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

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This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 27 and 31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Berkenstam et al. in view of Brunner et al. or Mochly-Rosen.

Applicants' invention is as described in the above 35 USC 102(e) rejection. In addition, applicants claim that the candidate molecule can be a peptide or small molecule.

Berkenstam et al. is as applied in the above 35 USC 102(e) rejection. Berkenstam et al. does not specifically teach that the candidate compound to be tested is a peptide or small molecule.

Brunner et al. and Mochly-Rosen teach that peptides and small molecules are common molecules that are routinely screened in assays to identify biologically active molecules that bind to target sites in cells. It is noted that the two cited references are among hundreds of similar references that recite screening assays where candidate molecules to be tested include peptides and small molecules.

The ordinary skilled artisan, seeking to choose candidate molecules to test in a method of identifying compounds that modulate a transcriptional response in a cell, would have been motivated to combine the teachings of Berkenstam et al. on methods of identifying compounds that modulate a transcriptional response to hypoxia with the teachings of Brunner et al. or Mochly-Rosen on the routine selection of peptides and small molecules as candidate molecules in various screening assays to identify compounds that bind to different target sites in cells because peptides and small molecules are commonly chosen as candidate molecules in screening assays. It would have been obvious for the ordinary skilled artisan to screen small molecules and peptides in the method disclosed by Berkenstam et al. because peptides and small molecules are ubiquitous, often have significant biological activities and are routinely chosen as candidate compounds to assay in screening methods. Given the teachings of the cited prior art and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered that said skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

### **Claim Objections**

Claim 5 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent form. Claim 5 recites the method of claim 1 wherein the cell is a cultured cell (i.e. *in vitro*). Claim 1 however

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recites an *in vivo* method of identifying a compound that modulates a transcriptional response to hypoxia. It is unclear how an *in vivo* testing method involves cultured cells.

Claim 7 is objected to. In Claim 7, the word "are" needs to be inserted between the words "exposed" and "induced" in line 2.

Claims 1-4, 6, 25 and 32 are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David Guzo, Ph.D., whose telephone number is (571) 272-0767. The examiner can normally be reached on Monday-Thursday from 8:00 Am to 5:30 PM. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Irem Yucel, Ph.D., can be reached on (571) 272-0781. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).



DAVID GUZO  
PRIMARY EXAMINER

David Guzo  
March 8, 2005